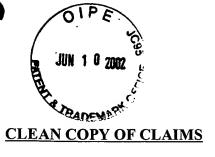
Serial No. 09/270,910 Docket No.: 4305/1E44-US1



- 2. A recombinant allergen according to claim 48, obtainable by
- a) identifying amino acid residues in a naturally occurring allergen which are conserved with more than 70% identity in all known of the homologous proteins within the taxonomic order from which said naturally occurring allergen originates;
- b) defining at least one patch of conserved amino acid residues being coherently connected over at least 400 Å² of the surface of the three-dimensional structure of the naturally occurring allergen molecule as defined by having a solvent accessibility of at least 20%, said at least one patch comprising at least one B cell epitope; and
- c) substituting at least one amino acid residue in said at least one patch with another non-conservative amino acid, wherein the α -carbon backbone tertiary structure of the allergen molecule is conserved.
- 3. A recombinant allergen according to claim 48, wherein the specific IgE binding to the mutant allergen is reduced by at least 5%, preferably at least 10%.
- 4. A recombinant allergen according to claim 48, wherein the average root mean square deviation of the atomic coordinates comparing the α -carbon backbone tertiary structures of the mutant and the naturally occurring allergen molecules is below 2Å.
- 5. A recombinant allergen according to claim 2, wherein said at least one patch consists of at least 15 amino acid residues.
- 6. A recombinant allergen according to claim 2, wherein the amino acid residues of said at least one patch are ranked with respect to solvent accessibility, and one or more amino acids among the more solvent accessible ones are substituted.

- 7. A recombinant allergen according to claim 6, wherein one or more amino acid residues of said at least one patch having a solvent accessibility of 20-80% are substituted.
- 8. A recombinant allergen according to claim 2, wherein 1-5 amino acid residues per 400Å² in said at least one patch are substituted.
- 9. A recombinant allergen according to claim 2, wherein the substitution of one or more amino acid residues in said B cell epitope or said at least one patch is carried out by site-directed mutagenesis.
- 10. A recombinant allergen according claim 48, wherein the allergen is derived from an inhalation allergen.
- 11. A recombinant allergen according to claim 10, wherein the allergen is derived from a pollen allergen.
- 12. A recombinant allergen according to claim 10, wherein the allergen is derived from a pollen allergen originating from the taxonomic order of *Fagales*, *Oleales* or *Pinales*.
- 13. A recombinant allergen according to claim 12, wherein the allergen is derived from *Bet v 1*.
- 14. A recombinant allergen according to claim 13, wherein at least one amino acid residue of said B cell epitope or said at least one patch is substituted.
- 16. A recombinant allergen according to claim 11, wherein the allergen is derived from a pollen allergen originating from the taxonomic order of *Poales*.
 - 17. A recombinant allergen according to claim 11, wherein the allergen is derived

from a pollen allergen originating from the taxonomic order of Asterales or Urticales.

- 18. A recombinant allergen according to claim 10, wherein the allergen is derived from a house dust mite allergen.
- 19. A recombinant allergen according to claim 18, wherein the allergen is derived from a mite allergen originating from *Dermatophagoides*.
- 20. A recombinant allergen according to claim 10, wherein the allergen is derived from a cockroach allergen.
- 21. A recombinant allergen according to claim 10, wherein the allergen is derived from an animal allergen.
- 22. A recombinant allergen according to claim 21, wherein the allergen is derived from an animal allergen originating from a cat, dog or horse.
- 23. A recombinant allergen according to claim 48, wherein the allergen is derived from a venom allergen.
- 24. A recombinant allergen according to claim 23 wherein the allergen is derived from a venom allergen originating from the taxonomic order of *Hymenoptera*.
- 25. A recombinant allergen according to claim 24 wherein the allergen is derived from a venom allergen from the taxonomic order of Vespidae, Apidae and Formicoidae.
- 26. A recombinant allergen according to claim 23, wherein the allergen is derived from Ves v 5.

- 27. A recombinant allergen according to claim 23, wherein at least one amino acid is substituted.
- 28. A recombinant allergen according to claim 25, wherein the substitution is from Lys to Ala at position 72 or from Tyr to Ala at position 96.
 - 32. A recombinant allergen according to claim 48 for use as a pharmaceutical.
- 33. A pharmaceutical composition, comprising a recombinant allergen according to claim 48, optionally in combination with a pharmaceutically acceptable carrier and/or excipient, and optionally an adjuvant.
- 34. A pharmaceutical composition according to claim 33, in the form of a vaccine against allergic reactions elicited by a naturally occurring allergen in patients suffering from allergy.
- 47. A pharmaceutical composition obtainable by the process according to claim 33.
- 48. A recombinant mutant allergen derived from a naturally occurring allergen in which at least one surface-exposed, amino acid residue of a B cell epitope at a position which is conserved in the amino acid sequences of homologous proteins within the taxonomic order from which the naturally occurring allergen originates, is substituted with an amino acid residue which is not conserved in the same position in the amino acid sequences of homologous proteins within the taxonomic order from which the naturally occurring allergen originates, wherein the α -carbon backbone tertiary structure of the recombinant allergen is conserved as compared with the α -carbon backbone tertiary structure of the naturally occurring allergen, and specific IgE binding to the mutant allergen is reduced compared to the IgE binding to the naturally occurring allergen.

- 49. A recombinant allergen according to claim 48, wherein the average root mean square deviation of the atomic coordinates comparing the α -carbon backbone tertiary structures of the mutant and the naturally occurring allergen molecules is below 2Å.
 - 50. A recombinant allergen according to claim 14 wherein said allergen has one or more an amino acid substitutions selected from the group consisting of:
 - (i) Thr at position 10 of SEQ ID NO: 37 substituted with Pro;
 - (ii) Asp at position 25 of SEQ ID NO: 37 substituted with Gly;
 - (iii) Asn at position 28 of SEQ ID NO: 37 substituted with Thr, and Lys at position 32 of SEQ ID NO: 37 substituted with Gln;
 - (iv) Glu at position 45 of SEQ ID NO: 37 substituted with Ser;
 - (v) As at position 47 of SEQ ID NO: 37 substituted with Ser;
 - (vi) Lys at position 55 of SEQ ID NO: 37 substituted with Asn;
 - (vii) Thr at position 77 of SEQ ID NO: 37 substituted with Ala;
 - (viii) Pro at position 108 of SEQ ID NO: 37 substituted with Gly; and
 - (ix) Asn at position 28 of SEQ ID NO: 37 substituted with Thr, Lys at position 32 of SEQ ID NO: 37 substituted with Gln, Glu at position 45 of SEQ ID NO: 37 substituted with Ser and Pro at position 108 of SEQ ID NO: 37 substituted with Gly.
- 51. A recombinant allergen according to claim 5, wherein said at least one patch consists of 15-25 amino acid residues.